

EXHIBIT B



U.S. Department of Justice

Michael K. Loucks
Acting United States Attorney
District of Massachusetts

Main Reception: (617) 748-3100

John Joseph Moakley United States Courthouse
Suite 9200
1 Courthouse Way
Boston, Massachusetts 02210

August 31, 2009

Brien T. O'Connor
Ropes & Gray LLP
One International Place
Boston, MA 02110

Re: United States v. Pharmacia & Upjohn Company, Inc.

Dear Mr. O'Connor:

This letter sets forth the Agreement between the United States Attorney for the District of Massachusetts ("the U.S. Attorney") and the United States Department of Justice (collectively, the United States Attorney and the United States Department of Justice will be referred to as the "United States") and your client, Pharmacia & Upjohn Company, Inc. (hereinafter "Pharmacia"), in the above-captioned case. The Agreement is as follows:

1. Change of Plea

At the earliest practicable date, Pharmacia shall waive indictment and plead guilty to the one-count Information attached hereto as Exhibit A, charging Pharmacia with a violation of the Food, Drug and Cosmetic Act, Title 21, U.S.C. Sections 331(a), 333(a)(2) and 352(f)(1). Pharmacia expressly and unequivocally admits that it knowingly, intentionally and willfully committed the crime charged in the attached Information and is in fact guilty of the offense, and agrees that it will not make any statements inconsistent with this explicit admission. Pharmacia agrees to waive venue, any applicable statutes of limitations, and any legal or procedural defects in the Information.

2. Penalties

Pharmacia faces the following maximum penalties on the count of conviction:

- (1) a maximum possible fine of \$500,000, twice the gross gain derived from the offense, or twice the gross loss to a person other than Pharmacia, whichever is greatest. See 18 U.S.C. §§ 3571(c), (d). The gross gain resulting from the offense

is \$664,000,000 and thus the maximum possible fine is \$1,328,000,000.

- (2) a term of probation of not less than one (1) year and not more than five (5) years. *See* 18 U.S.C. § 3561(c)(1).
- (3) a special assessment in the amount of \$400. *See* 18 U.S.C. § 3013(a)(2)(B).
- 3. Sentencing Guidelines

The parties agree to take the following positions at sentencing under the United States Sentencing Guidelines:

- a. The parties agree that the Guideline Manual in effect as of the date of sentencing should be used in determining Pharmacia's sentence. *See* U.S.S.G. § 1B1.11(a);
- b. The parties agree that the base fine is \$664,000,000, which is the pecuniary gain to the organization from the offense. *See* U.S.S.G. §§ 8C2.3 and 8C2.4(a);
- c. Pursuant to U.S.S.G. § 8C2.5, the culpability score is eight (8) determined as follows:
 - (1) Base culpability score is five (5) pursuant to U.S.S.G. § 8C2.5(a);
 - (2) Add five (5) points pursuant to U.S.S.G. § 8C2.5(b)(1)(A), in that the organization had 5,000 or more employees, and an individual within the high-level personnel of the unit participated in or condoned the offense and/or tolerance of the offense by substantial authority personnel was pervasive throughout the organization;
 - (3) Deduct two (2) points for Pharmacia's full cooperation pursuant to U.S.S.G. § 8C2.5(g)(2).
- d. Pursuant to U.S.S.G. § 8C2.6, the appropriate multiplier range associated with a culpability score of eight (8) is 1.6 to 3.2;
- e. Thus, the Guideline Fine Range is \$1,062,400,000 to \$1,328,000,000. *See* U.S.S.G. §§ 8C2.7(a), (b); 18 U.S.C. §§ 3571(c) and (d); and,
- f. The parties agree that (1) disgorgement pursuant to U.S.S.G. § 8C2.9 is not necessary, (2) there is no basis for a downward departure or deviation under the

United States Sentencing Guidelines and (3) a fine within the guideline range will result in a reasonable sentence taking into consideration all of the factors set forth in 18 U.S.C. §§ 3553(a), 3572.

4. Agreed Disposition

The United States and Pharmacia agree pursuant to Fed. R. Crim. P. 11(c)(1)(C) that the following sentence is the appropriate disposition of the Information:

- a. a criminal fine in the amount of one billion one hundred ninety-five million dollars (\$1,195,000,000) to be paid within one week of the date of sentencing;
- b. a mandatory special assessment of \$400 pursuant to 18 U.S.C. § 3013, which shall be paid to the Clerk of Court on or before the date of sentencing; and
- c. criminal forfeiture in the amount of \$105,000,000;
- d. In light of the pending civil action, *United States ex rel. Kopchinski v Pfizer, et. al.*, C.A. No. 05-CV-12115 (D. Mass.) (the "Civil Action"), and the Civil Settlement Agreement between Pfizer Inc and the United States relating to the Civil Action which is being signed contemporaneously with this plea agreement, and attached hereto as Exhibit B, which requires the payment of \$1,000,000,000, plus interest, and in light of the October 17, 2008 agreements in principle reached by Pfizer Inc resolving substantially all personal injury and class action cases alleging that Pfizer's pain medication Bextra was the cause of injury, it appears that a process is in place under which all identifiable victims will have the opportunity to be fully recompensed. The private payor victims will have been recompensed from the agreements in principle reached by Pfizer Inc with the personal injury plaintiffs, and the loss suffered by the federal program victims will be recompensed through the Federal Settlement Amount as defined in the Civil Settlement Agreement. Therefore, the United States agrees that it will not seek a separate restitution order as to Pharmacia as part of the resolution of the Information and the parties agree that the appropriate disposition of this case does not include a restitution order. The parties further agree that any attempt to further effect restitution would unduly complicate and prolong the sentencing to the degree that the benefit to any further victims would outweigh the burden on the sentencing process under 18 U.S.C. § 3663(a)(1)(B)(ii).

The United States specifically may, at its sole option, be released from its commitments under this Agreement, including, but not limited to, its agreement that this paragraph constitutes the appropriate disposition of this case, if at any time between its execution of this Agreement and sentencing, Pharmacia:

- (a) Fails to admit a complete factual basis for the plea;
- (b) Fails to truthfully admit its conduct in the offense of conviction;
- (c) Falsely denies, or frivolously contests, relevant conduct for which Pharmacia is accountable under U.S.S.G. § 1B1.3;
- (d) Gives false or misleading testimony in any proceeding relating to the criminal conduct charged in this case and any relevant conduct for which Pharmacia is accountable under U.S.S.G. § 1B1.3;
- (e) Engages in acts which form a basis for finding that Pharmacia has obstructed or impeded the administration of justice under U.S.S.G. § 3C1.1;
- (f) Attempts to withdraw its plea.

Pharmacia expressly understands that it may not withdraw its plea of guilty, unless the Court rejects this Agreement under Fed. R. Crim. P. 11(c)(5).

5. No Further Prosecution of Pharmacia

Pursuant to Fed. R. Crim. P. 11(c)(1)(A), the United States agrees that, other than the charges in the attached Information, it shall not further prosecute Pharmacia for conduct relating to the drug Bextra which (a) falls within the scope of the Information; (b) was a subject of the investigation by the grand jury; or (c) was known to the U.S. Attorney prior to January 23, 2009. This declination is expressly contingent on:

- (1) the guilty plea of Pharmacia being accepted by the Court and not withdrawn; and
- (2) Pharmacia's performance of all of its material obligations as set forth in this Agreement and Pfizer's performance of all of its material obligations set forth in the attached Civil Settlement Agreement. If Pharmacia's guilty plea is not accepted by the Court or is withdrawn for any reason, or if Pharmacia should fail to perform a material obligation under this Agreement, or if Pfizer should fail to perform a material obligation under the Civil Settlement Agreement, this declination of prosecution shall be null and void.

The United States expressly reserves the right to prosecute any individual, including but not limited to present and former officers, directors, employees, and agents of Pharmacia, in connection with the conduct encompassed by this plea agreement, within the scope of the grand jury investigation, or known to the U.S. Attorney.

6. Payment of Mandatory Special Assessment

Pharmacia agrees to pay the mandatory special assessment to the Clerk of the Court on or before the date of sentencing.

7. Waiver of Rights to Appeal and to Bring Collateral Challenge

Pharmacia is aware that it has the right to challenge its sentence and guilty plea on direct appeal. Pharmacia is also aware that it may, in some circumstances, be able to argue that its plea should be set aside, or its sentence set aside or reduced, in a collateral challenge such as pursuant to a motion under 28 U.S.C. § 2255.

In consideration of the concessions made by the United States in this Agreement, Pharmacia knowingly and voluntarily waives its right to appeal or collaterally challenge:

- (a) Pharmacia's guilty plea and any other aspect of Pharmacia's conviction, including, but not limited to, any rulings on pretrial suppression motions or any other pretrial dispositions of motions and issues; and
- (b) The imposition by the District Court of the sentence agreed to by the parties, as set out in paragraph 4, even if the Court rejects one or more positions advocated by the parties with regard to the application of the U.S. Sentencing Guidelines.

Pharmacia's waiver of rights to appeal and to bring collateral challenges shall not apply to appeals or challenges based on new legal principles in First Circuit or Supreme Court cases decided after the date of this Agreement which are held by the First Circuit or Supreme Court to have retroactive effect.

This Agreement does not affect the rights or obligations of the United States as set forth in 18 U.S.C. § 3742(b), and the U.S. Attorney therefore retains his appeal rights.

8. Fed. R. Crim. P. 11(c)(1)(C) Agreement

Pharmacia's plea will be tendered pursuant to Fed. R. Crim. P. 11(c)(1)(C). Pharmacia cannot withdraw its plea of guilty unless the sentencing judge rejects this Agreement or fails to impose a sentence consistent herewith. If the sentencing judge rejects this Agreement or fails to impose a sentence consistent herewith, this Agreement shall be null and void at the option of either the United States or Pharmacia.

Pharmacia may seek sentencing by the Court immediately following the Rule 11 plea hearing. The United States does not object to the Court sentencing Pharmacia immediately following the Rule 11 plea hearing or prior to the completion of a Presentence Report. Pharmacia understands that the decision whether to proceed immediately following the plea

hearing with the sentencing proceeding, and to do so without a Presentence Report, is exclusively that of the United States District Court.

9. Cooperation

Pharmacia shall cooperate completely and truthfully in any trial or other proceeding arising out of any ongoing civil, criminal or administrative investigation of its current and former officers, agents, employees and customers in connection with matters described in the Information. Pharmacia shall make reasonable efforts to facilitate access to, and to encourage the cooperation of, its current and former officers, agents, and employees for interviews sought by law enforcement agents, upon request and reasonable notice in connection with matters described in the Information. Pharmacia shall also take reasonable measures to encourage its current and former officers, agents, and employees to testify truthfully and completely before any grand jury, and at any trial or other hearing, at which they are requested to do so by any government entity in connection with matters described in the Information.

In addition, Pharmacia shall promptly furnish to law enforcement agents, upon request, all documents and records in its possession, custody or control relating to the conduct that is within the scope of any such ongoing federal investigation, trial or other proceeding in connection with matters described in the Information, and that are not covered by the attorney-client privilege or work product doctrine.

Provided, however, notwithstanding any provision of this Agreement, that: (1) Pharmacia is not required to request of its current or former officers, agents, or employees that they forego seeking the advice of an attorney or that they act contrary to that advice; (2) Pharmacia is not required to take any action against its officers, agents, or employees for following their attorney's advice; and (3) Pharmacia is not required to waive any privilege or claim of work product protection.

10. Probation Department Not Bound By Agreement

The sentencing disposition agreed upon by the parties and their respective calculations under the Sentencing Guidelines are not binding upon the United States Probation Office.

11. Forfeiture

Pharmacia will forfeit to the United States assets subject to forfeiture pursuant to 21 U.S.C. § 334 and 28 U.S.C. § 2461(c) as a result of its guilty plea. Pharmacia admits that the value of the quantities of Bextra which were misbranded in violation of 21 U.S.C. § 331 totaled at least \$105,000,000.00 in United States currency. Pharmacia acknowledges and agrees that the quantities of Bextra which were misbranded in violation of 21 U.S.C. § 331 cannot be located upon exercise of due diligence, or have been transferred or sold to, or deposited with, a third party, placed beyond the jurisdiction of the Court, substantially diminished in value, or commingled with other property which cannot be divided without difficulty. Accordingly,

Pharmacia agrees that the United States is entitled to forfeit as “substitute assets” any other assets of Pharmacia up to the value of the now missing directly forfeitable assets.

Pharmacia agrees that, no later than one week after sentencing, it shall remit the amount of \$105,000,000 in United States currency to the United States Marshals Service pursuant to the wire instructions provided by the United States Attorney’s Office. Pharmacia and the United States agree that this payment shall satisfy any and all forfeiture obligations that Pharmacia may have as a result of its guilty plea.

Forfeiture of substitute assets shall not be deemed an alteration of Pharmacia’s sentence. The forfeitures set forth herein shall not satisfy or offset any fine, restitution, cost of imprisonment, or other penalty imposed upon Pharmacia, nor shall the forfeitures be used to offset Pharmacia’s tax liability or any other debt owed to the United States.

Pharmacia agrees to consent to the entry of orders of forfeiture for the \$105,000,000.00 in United States currency, and waives the requirements of Federal Rules of Criminal Procedure 32.2 and 43(a) regarding notice of the forfeiture in the charging instrument, entry of a preliminary order of forfeiture, announcement of the forfeiture at sentencing, and incorporation of the forfeiture in the judgment. Pharmacia acknowledges that it understands that the forfeiture of assets is part of the sentence that may be imposed in this case and waives any failure by the court to advise it of this, pursuant to Rule 11(b)(1)(J), at the time the guilty plea is accepted.

In addition to all other waivers or releases set forth in this Agreement, Pharmacia hereby waives any and all claims arising from or relating to the forfeitures set forth in this section, including, without limitation, any claims arising under the Double Jeopardy Clause of the Fifth Amendment, or the Excessive Fines Clause of the Eighth Amendment, to the United States Constitution, or any other provision of state or federal law.

The United States District Court for the District of Massachusetts shall retain jurisdiction to enforce the provisions of this section.

12. Civil and Administrative Liability

By entering into this Agreement, the United States does not compromise any civil liability, including but not limited to any False Claims Act or tax liability, which Pharmacia may have incurred or may incur as a result of its conduct and its plea of guilty to the attached Information.

Pharmacia’s civil liability to the United States in connection with certain matters under investigation by the United States is resolved in the Civil Settlement Agreement with Pfizer Inc, attached as Exhibit B, according to the terms set forth in that Agreement.

13. Waiver of Defenses

If Pharmacia's guilty plea is not accepted by the Court for whatever reason, or is later withdrawn for whatever reason, Pharmacia hereby waives, and agrees it will not interpose, if charges are filed within six months of the date on which such guilty plea is rejected or withdrawn, any defense to any charges brought against it which it might otherwise have for pre-indictment delay, any statute of limitations, or the Speedy Trial Act, except any such defense that Pharmacia may have for conduct occurring prior to November 15, 2000.

14. Breach of Agreement

If the United States determines that Pharmacia has failed to comply with any provision of this Agreement, or has committed any crime following its execution of this Agreement, the United States may, at its sole option, be released from its commitments under this Agreement in its entirety by notifying Pharmacia, through counsel or otherwise, in writing. The United States may also pursue all remedies available to it under the law, even if it elects not to be released from its commitments under this Agreement. Pharmacia recognizes that no such breach by it of an obligation under this Agreement shall give rise to grounds for withdrawal of its guilty plea. Pharmacia understands that, should it breach any provision of this agreement, the United States will have the right to use against Pharmacia before any grand jury, at any trial or hearing, or for sentencing purposes, any statements which may be made by it, and any information, materials, documents or objects which may be provided by it to the government subsequent to this Agreement, without any limitation.

Pharmacia understands and agrees that this 11(c)(1)(C) plea agreement and its agreed upon criminal disposition:

- a. are wholly dependent upon Pfizer's timely compliance with the material provisions of the attached Civil Settlement Agreement; and that
- b. failure by Pharmacia to comply fully with the material terms of this Agreement or by Pfizer to comply fully with the material terms of the attached Civil Settlement Agreement, including the payments required therein, will constitute a breach of this Agreement, provided however, that a breach of the Corporate Integrity Agreement (the "CIA"), referred to in the Civil Settlement Agreement, does not constitute a breach of this Plea Agreement, and any disputes arising under the CIA shall be resolved exclusively through the dispute resolution provisions of the CIA.

In the event Pharmacia at any time hereafter breaches any material provision of this Agreement, Pharmacia understands that (1) the United States will as of the date of that breach be relieved of any obligations it may have in this Agreement and the attached Civil Settlement Agreement, including but not limited to the promise not to further prosecute Pharmacia as set forth in paragraph 5 of this Agreement; and (2) Pharmacia will not be relieved of its obligation to make the payments set forth in this Agreement and Pfizer will not be relieved of its obligation to

make the payments set forth in the attached Civil Settlement Agreement, nor will it be entitled to return of any monies already paid. Moreover, in the event of a material breach, Pharmacia, with respect to any charges which could have been brought as of the date of this letter, and are brought within six months of the declaration of a breach, hereby waives, and agrees it will not interpose, any defense to any charges brought against it which it might otherwise have for pre-indictment delay, any statute of limitations, or the Speedy Trial Act, except any such defense that Pharmacia may already have for conduct occurring before November 15, 2000.

15. Who Is Bound By Agreement

With respect to matters set forth in Paragraph 5, this Agreement is binding among Pharmacia and the Office of the United States Attorney for the District of Massachusetts, the United States Attorney's Offices for each of the other 93 judicial districts of the United States, and the Office of Consumer Litigation of the Department of Justice. The non-prosecution provisions in Paragraph 5 are also binding on the Criminal Division of the United States Department of Justice, with the exception of the investigation of Pharmacia being conducted by the Fraud Section of the Criminal Division regarding possible violations of the Foreign Corrupt Practices Act and related offenses in connection with the sales and marketing of Pharmacia's products to foreign customers, which investigation is specifically excluded from the release in Paragraph 5. A copy of the letter to Acting United States Attorney Michael K. Loucks from the Deputy Assistant Attorney General, Criminal Division, U.S. Department of Justice, authorizing this Agreement is attached as Exhibit C. Pharmacia understands that this Agreement does not bind any state or local prosecutorial authorities, the Tax Division of the U.S. Department of Justice, or the Internal Revenue Service of the U.S. Department of the Treasury.

16. Corporate Authorization

Pharmacia's acknowledgment of this Agreement and execution of this Agreement on behalf of the corporation is attached as Exhibit D. Pharmacia shall provide to the U.S. Attorney and the Court a certified copy of a resolution of the Board of Directors of Pharmacia Corporation, affirming that the Board of Directors has authority to enter into the Plea Agreement and has (1) reviewed the Information in this case and the proposed Plea Agreement or has been advised of the contents thereof; (2) consulted with legal counsel in connection with the matter; (3) voted to enter into the proposed Plea Agreement; (4) voted to authorize Pharmacia to plead guilty to the charge specified in the Information; and (5) voted to authorize the corporate officer identified below to execute the Plea Agreement and all other documents necessary to carry out the provisions of the Plea Agreement. A copy of the resolution is attached as Exhibit E. Pharmacia agrees that either a duly authorized corporate officer or a duly authorized attorney for Pharmacia, at the discretion of the Court, shall appear on behalf of Pharmacia and enter the guilty plea and will also appear for the imposition of sentence.

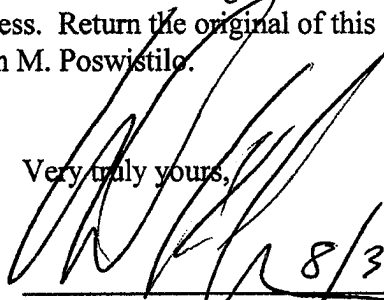
17. Complete Agreement

This Agreement, together with the Civil Settlement Agreement, set forth the complete and only agreement between the parties relating to the disposition of this matter. No promises,

representations or agreements have been made other than those set forth in this letter and its attachments A through E. This Agreement supersedes prior understandings, if any, of the parties, whether written or oral. This Agreement can be modified or supplemented only in a written memorandum signed by the parties or on the record in court.

If this letter accurately reflects the Agreement between the U.S. Attorney and your client, Pharmacia, please have the authorized representative of Pharmacia sign the Acknowledgment of Agreement below. Please also sign below as Witness. Return the original of this letter to Assistant U.S. Attorneys Sara M. Bloom and Susan M. Poswistilo.

Very truly yours,

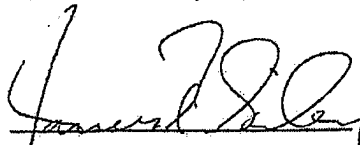

8/31/9
MICHAEL K. LOUCKS
Acting United States Attorney

ACKNOWLEDGMENT OF PLEA AGREEMENT

The Board of Directors has authorized me to execute this Plea Agreement on behalf of Pharmacia & Upjohn Company, Inc. The Board has read this Plea Agreement, the attached criminal information, and the Civil Settlement Agreement including its attachment in their entirety, or has been advised of the contents thereof, and has discussed them fully in consultation with Pharmacia & Upjohn Company, Inc.'s attorneys. I am further authorized to acknowledge on behalf of Pharmacia & Upjohn Company, Inc. that these documents fully set forth Pharmacia & Upjohn Company, Inc.'s agreement with the United States, and that no additional promises or representations have been made to Pharmacia & Upjohn Company, Inc. by any officials of the United States in connection with the disposition of this matter, other than those set forth in these documents.

Dated:

Aug 20th, 2009


Vice President and Secretary
Pharmacia & Upjohn Company, Inc.

Dated:

BRIEN T. O'CONNOR
Ropes & Gray LLP
Counsel for Pharmacia & Upjohn Company, Inc.

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Dated:

James Gibney
Vice President and Secretary
Pharmacia & Upjohn Company, Inc.

Dated:

8/31/09

BRIEN T. O'CONNOR
Ropes & Gray LLP
Counsel for Pharmacia & Upjohn Company, Inc.

)	Criminal No.
UNITED STATES OF AMERICA,)	
)	
v.)	21 U.S.C. §§ 331(a), 333(a)(2)
PHARMACIA & UPJOHN COMPANY, INC.)	and 352 (Introduction into
Defendant.)	Interstate Commerce of a
)	Misbranded Drug)

The United States Attorney charges that:

At all times material to this Information, unless otherwise alleged:

2. Prior to the April 2003 acquisition, Pharmacia Corporation and its subsidiaries, including **PHARMACIA INC.**, jointly promoted the drug Bextra with Pfizer Inc. Since April 2003, Pharmacia Corporation and Pharmacia Inc. have been wholly owned subsidiaries of Pfizer Inc.

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3. **PHARMACIA INC.** holds the United States trademarks and patents for the drug Bextra, which was distributed from Puerto Rico into interstate commerce throughout the United States, including specifically into Massachusetts, from in or about February 2002 until approximately April 2005.

The FDA and the FDCA

4. The United States Food and Drug Administration (“FDA”) was the federal agency of the United States responsible for protecting the health and safety of the public by enforcing the Federal Food, Drug and Cosmetic Act, (“FDCA”), 21 United States Code, Section 301, *et seq.*, and ensuring, among other things, that drugs intended for use in humans were safe and effective for each of their intended uses and that the labeling of such drugs bore true and accurate information.

5. The FDCA, and its implementing regulations, required that, with certain exceptions not relevant here, before a new drug could legally be introduced into interstate commerce, a sponsor of a new drug submit and obtain approval of a New Drug Application (“NDA”) from the FDA.

6. The FDCA required that the NDA include proposed labeling for the proposed intended uses of the drug which included, among other things, the conditions for therapeutic use. The NDA was also required to contain, to the satisfaction of FDA, data generated in adequate and well-controlled clinical trials that demonstrated that the drug would be safe and effective when used in accordance with the proposed labeling.

7. An NDA sponsor was not permitted to promote and market a new drug until it had an approved NDA, including approval for the proposed labeling. Moreover, if approved, the

sponsor was permitted to promote and market the drug only for the medical conditions of use and dosages specified in the approved labeling. Uses not approved by the FDA, including dosages not approved in the drug's approved labeling, were known as "unapproved" or "off-label" uses.

8. The FDCA, and its implementing regulations, required the sponsor to file a Supplemental NDA ("sNDA"), in order to label or promote a drug for uses and dosages different from the conditions for use and dosage specified in the approved labeling. The sNDA was required to include a description of the newly proposed indications for use, and evidence consisting of well-controlled clinical studies, sufficient to demonstrate that the drug was safe and effective for the new use or uses. Only upon FDA approval of the sNDA could the sponsor promote the drug for the new intended use.

9. The FDCA provided that, unless otherwise exempted, a drug was misbranded if, among other things, the labeling did not contain adequate directions for use. 21 U.S.C. § 352(f)(1). Adequate directions for use could not be written for medical indications or uses for which the drug had not been approved and proven to be safe and effective through well-controlled clinical studies because unapproved uses could not be included in the labeling. Drugs that were promoted for uses that had not been approved by the FDA were deemed to be misbranded under Section 352(f)(1).

10. The FDCA prohibited the delivery for introduction and causing the delivery for introduction into interstate commerce of a misbranded drug.

The Bextra Approval Process

11. Bextra was PHARMACIA's trade name for the drug valdecoxib that was a so-called "Cox-2 Inhibitor." At the time Bextra first came on the market in February 2002, the

“Cox-2” class of drugs included the previously released drug Celebrex, also marketed by **PHARMACIA**, and Vioxx, manufactured and marketed by a competitor.

12. The Cox-2 class of drugs was designed to relieve various forms of pain and inflammation and was intended to offer pain relief equal to the predecessor pain relievers, but without the negative gastrointestinal side effects often associated with those drugs. Thus, for many patients, the justification for switching to a Cox-2 drug over the other available pain relievers was greater gastrointestinal safety, not better efficacy.

13. Because many of the other pain relievers, such as ibuprofen or naproxen, were available as generic and over-the-counter drugs at the time Bextra was launched, Bextra was much more expensive than the competitor drugs.

14. On or about January 15, 2001, **PHARMACIA** submitted an NDA seeking approval of Bextra, which was a new drug within the meaning of 21 U.S.C. § 321(p) and 21 C.F.R. §§ 310.3 (h)(4) and (5). In that NDA, **PHARMACIA** sought approval to market Bextra at dosages of 10 mg, 20 mg and 40 mg for the following uses:

- (1) For the prevention and treatment of acute pain in adults. Preoperative administration of [Bextra] prevents or reduces post-operative pain. [Bextra] has an opioid sparing effect when used concomitantly with opioids;
- (2) For the treatment of primary dysmenorrhea; and
- (3) For relief of signs and symptoms of osteoarthritis and adult rheumatoid arthritis.

The FDA Approval and Non-Approval of Bextra

15. On or about November 16, 2001, the FDA approved Bextra to treat the signs and symptoms of osteoarthritis (“OA”), adult rheumatoid arthritis (“RA”) and for the treatment of primary dysmenorrhea (“PD”). **PHARMACIA** sought approval of Bextra for general acute pain,

for the preemption of the pain of surgery, and for opioid sparing, but the FDA declined to grant such approvals.

16. Moreover, although **PHARMACIA** had sought approval for the 10 mg, 20 mg and 40 mg doses for all uses, the FDA only approved the 20 mg dose twice a day as needed for PD, and the FDA only approved the 10 mg dose once a day for OA and RA (hereinafter these uses for Bextra will be referred to throughout this Information as the “Approved Uses and Dosages”).

17. The FDA never approved Bextra for any use or dosage other than the Approved Uses and Dosages.

18. The FDA informed **PHARMACIA** that it was not approving Bextra for acute pain at least in part because of a safety concern about Bextra. The safety concern cited by the FDA was the results of a study of Bextra following the administration of its injectable form, parecoxib, used in patients undergoing coronary artery bypass graft surgery (the “CABG I” trial), in which the FDA noted that there was an excess of serious cardiovascular thromboembolic events in the Bextra (after parecoxib) arm of the trial.

19. In its comments to the proposed label for Bextra, the FDA also informed **PHARMACIA** that the FDA recommended against the use of 20 mg for treatment of arthritis based upon an increased potential for adverse events at higher dosages.

20. In or about October 2004, the results of a second study of Bextra and parecoxib in coronary artery bypass graft surgery (“CABG II”) became public. This study showed a statistically significant increase in thromboembolic cardiovascular events in CABG patients taking Bextra following the administration of parecoxib.

21. As a result of this study, in or about November 2004, a warning was added to Bextra's product label which stated that Bextra was contraindicated for treatment of post-operative pain following CABG surgery. At the same time, the FDA required a black box warning on Bextra's label about reports of serious skin reactions, including Stevens-Johnson syndrome, in patients receiving Bextra.

22. From in or about February 2002 through April 2005, **PHARMACIA** promoted the sale of Bextra, as set forth below, for uses and dosages other than the Approved Uses and Dosages and/or with false and misleading claims of safety and efficacy and without disclosing the FDA's safety concerns.

A. PHARMACIA's Promotion of Bextra for General Acute Pain

23. **PHARMACIA** marketed Bextra for acute pain, including surgical pain, and at unapproved doses, despite the FDA's specific refusal to approve Bextra for those uses, and without disclosing to physicians, customers and others that the FDA specifically declined to approve Bextra for those uses and doses, and that the FDA's refusal was due in part to a safety concern about potential serious adverse events including cardiovascular events in some surgeries based upon the results of the CABG I study.

24. From in or about November 2001 to in or about April 2005, **PHARMACIA's** marketing team positioned Bextra for *acute* pain to differentiate Bextra's use from that of **PHARMACIA's** existing drug Celebrex, which was often used for *chronic* conditions, and to take sales from its competitor's drug Vioxx, which was used by many physicians for acute pain, among other indications. In doing so, **PHARMACIA** sought to maximize Bextra sales while avoiding cannibalizing sales of **PHARMACIA's** existing Cox-2 drug, Celebrex.

25. **PHARMACIA's** headquarters marketing team created marketing messages and materials for the **PHARMACIA** sales force that promoted Bextra for unapproved uses and dosages, including materials that directed **PHARMACIA's** sales force to aggressively pursue written surgical and pain management standing orders for Bextra, including for uses for which Bextra was unapproved.

26. From in or about October 2002 to January 2003, and at other times, **PHARMACIA** marketing managers commissioned market research to test new promotional visual aids for Bextra to determine, among other things, whether the visual aids delivered the "intended message" of Bextra for "acute pain."

27. For example, on or about December 5, 2002, a **PHARMACIA** marketing manager for Bextra forwarded to senior **PHARMACIA** marketing managers a market research report that concluded that "almost all physicians clearly understood the intended use of Celebrex (for chronic pain) and Bextra (for acute pain)" and noted in the cover email that the visual aid clearly communicated the "intended message" that "Celebrex is for chronic pain; Bextra is for acute or tough to treat pain."

28. On or about March 24, 2003 and thereafter, **PHARMACIA** continued to promote Bextra for such unapproved uses and dosages despite the fact that a senior **PHARMACIA** manager of market analytics notified marketing managers that "the majority" of **PHARMACIA** sales representatives surveyed were using a "chronic/acute" or "persistent/acute" distinction to describe how the physician can use Celebrex and Bextra and noted that some of the representatives surveyed voiced "discomfort" in delivering this positioning of Celebrex for chronic and Bextra for acute pain, in light of the fact that Bextra had no acute pain indication.

29. In or about March 2003, **PHARMACIA** marketing managers, in a presentation to other **PHARMACIA** marketing managers, highlighted as a success factor the fact that **PHARMACIA** had promoted Bextra for acute pain and Celebrex for chronic pain and set forth as an opportunity for improvement the “Need to Emphasize Chronic Use of Celebrex, Acute use of Bextra.”

30. In or about August 2003, **PHARMACIA** commissioned a market research report to confirm that a visual aid it was preparing for sales representatives to promote Celebrex and Bextra. The report confirmed that the visual aid conveyed the message to physicians that **PHARMACIA** intended Bextra to be used for acute pain, and concluded that “[a]fter seeing the positioning statement for Bextra, virtually all physicians concluded that **PHARMACIA** was trying to differentiate Bextra as a product for acute pain.”

31. In or about September 2003, **PHARMACIA** again commissioned market research to be performed to confirm that the final version of the new visual aid conveyed **PHARMACIA**’s intended message for the use of Bextra. The report stated:

More so than in other research conducted by this moderator for this team to date, physicians are starting to extract a “chronic/long-term” message for Celebrex and an “acute” message for Bextra from the visual aid materials, which will likely become more apparent over time through continued exposure to the new visual aid.

32. **PHARMACIA** continued to promote Bextra for such unapproved uses and dosages even after senior marketing managers received this market research and internal reports that indicated that the sales force was promoting Bextra for unapproved uses and dosages.

B. PHARMACIA's Promotion of Bextra for Unapproved Uses Through Remuneration to Physicians and Purported Physician Consulting Arrangements

33. PHARMACIA also promoted Bextra for unapproved use and dosages by convening so-called advisory boards, consultant meetings and other fora. PHARMACIA targeted physicians to participate in these meetings, as part of what PHARMACIA termed a "cascade of influence" in order to turn high prescribing physicians into PHARMACIA Cox-2 "advocates."

34. As part of this process, PHARMACIA conducted what it terms "Influence Mapping" in which it conducted market research to identify "influential specialists in the areas of arthritis and pain" and to provide an "Advocate Concierge" or a "High level service to aid key Advocates in managing their interaction" with PHARMACIA. As part of this process, PHARMACIA ranked key physicians in terms of their ability to influence key professional societies, regulatory agencies, guideline committees, and specialty journals.

35. For example, PHARMACIA's 2002 planning documents described the 2002 activities that it planned to use to disseminate its Bextra messages, including National Advisory Boards, National Steering Committee Meetings, National Consultant Meetings and Regional Consultant Meetings, all in order to "Deliver Product Messages with Data Support for Both Brands" and "Maximize Cost Synergies & ROI [Return on Investment]."

36. As part of this process, PHARMACIA paid targeted physicians both airfare and two to three days' accommodations at lavish resorts in the Bahamas, Virgin Islands and across the United States, and further entertained these physicians with golf, massages and other recreational activities, and also paid them an honoraria in the range of \$1,000 to \$2,000 for their

attendance. The number of attendees at this event often ranged from 50 to 100 health care professionals.

37. Between late 2001 and late 2003, **PHARMACIA** held almost 100 of these so-called consultant meetings and thus promoted unapproved uses and dosages of Bextra to and entertained over 5,000 health care professionals.

38. In furtherance of these plans, **PHARMACIA** paid these physicians whom it had identified as these advocates to present at lunches, dinners, and other entertainment venues, where in many instances **PHARMACIA** thereby further spread its messages about unapproved uses and dosages of Bextra.

C. PHARMACIA's Promotion of Bextra for Surgical Pain

39. **PHARMACIA** managers instructed their sales teams to promote Bextra for the acute pain of surgery, both pre- and post-operatively, even though they knew that Bextra was not FDA- approved for these uses, and without disclosing to physicians, customers and others that the FDA specifically declined to approve Bextra for those uses and doses, and that the FDA's refusal was due in part to a safety concern about potential serious adverse events, including cardiovascular events, in some surgeries based upon the results of the CABG I study.

40. **PHARMACIA** managers trained and directed their sales teams to seek written surgical and pain management protocols, standing orders and pathways from physicians, hospitals, and other customers for use in pre- and post-operative surgical situations.

41. **PHARMACIA** managers circulated an electronic template of a hospital-wide pain management pathway that provided for administration of Bextra for unapproved uses and at unapproved dosages and gave instructions on how to get such pathways printed on laminated

color paper and distributed in hospitals and other institutions.

42. **PHARMACIA** managers encouraged their sales representatives to promote Bextra for unapproved uses and dosages by circulating examples of written protocols obtained by other representatives that called for unapproved uses and dosages of Bextra in certain surgical and pain management settings.

43. **PHARMACIA** managers held contests to encourage the preparation and promotion of such protocols and praised and rewarded representatives who obtained such surgical and pain management protocols for unapproved uses and dosages of Bextra.

44. Consistent with these instructions and incentives, **PHARMACIA's** sales team promoted, drafted and distributed to physicians written protocols, pain management pathways and standing orders for Bextra for uses and dosages that they knew were not FDA-approved.

45. For example, in or about June or July 2002, a **PHARMACIA** sales representative in Massachusetts drafted and recommended a written protocol to an OB/GYN physician in Massachusetts calling for the unapproved use of Bextra to control pain in OB/GYN surgeries, including at unapproved dosages.

46. On or about July 19, 2002, a **PHARMACIA** Regional Manager sent an email to sales representatives in the Northeast region praising the sales representative for a "fantastic protocol" in six areas of OB/GYN surgery, each an unapproved use for Bextra.

47. On or about February 19, 2003, a **PHARMACIA** District Manager sent an email to the sales representatives in the district, with a copy to a Regional Manager that instructed the representatives to sell Bextra for pre- and post-operative pain to orthopedic surgeons, podiatrists, oral surgeons, and "anyone that uses a scalpel for a living."

48. On or about June 19, 2003, a **PHARMACIA** District Manager emailed a sample pre-operative briefing sheet to sales representatives to use, with a copy to the Regional Manager, which provided for the use of 10 mg and 20 mg of Bextra once or twice a day as part of the pre-operative surgery instructions, without any limit to Bextra's Approved Uses or Dosages.

49. In the June 19, 2003 email, a **PHARMACIA** District Manager praised the efforts of the sales representative who drafted, promoted and persuaded a physician to adopt the above briefing sheet and awarded the representative "ACE" points, which are points that could be used to select prizes such as trips, gift certificates and appliances from a **PHARMACIA** awards catalog.

50. On or about July 25, 2003, a **PHARMACIA** District Manager circulated to the Regional Manager in his district and district managers in other districts an "OPERATE FOR CASH" contest, in which sales representatives could earn ACE points by implementing Bextra written standing orders and protocols with individual orthopedic surgeons, hospital-wide, or in surgical departments.

51. On or about August 26, 2003, a **PHARMACIA** District Manager sent an email, with a copy to the Regional Manager, that instructed sales representatives to promote Bextra and Celebrex for pre- and post-operative pain, reminded them about the Operate for Cash contest, and suggested the representatives focus on "low hanging fruit," such as oral surgeons, periodontists and dentists, none of whom would have an FDA-approved use for Bextra.

D. PHARMACIA's Off-Label Promotion of Bextra for Prevention of Deep Vein Thrombosis ("DVTs")

52. **PHARMACIA** caused members of its sales force to promote Bextra with the claim that Bextra was effective in the surgical setting to reduce the risk of blood clots known as DVTs that can form during or after surgery. In promoting Bextra to reduce the risk of DVTs, **PHARMACIA** representatives did not disclose that the FDA specifically refused to approve Bextra for the treatment of pre- and post-operative surgical pain, and that the FDA had concluded that the safety and efficacy of Bextra for such use had not been established, including specifically that a reduction of side effects (such as DVT's) had not been shown in the studies. As **PHARMACIA** knew, there were no scientific studies showing that Bextra was safe or effective to reduce the risk of DVTs.

53. Thus, on or about April 24, 2002, a **PHARMACIA** Regional Manager sent an email to sales representatives and managers in the division, including numerous representatives and managers, and instructed them (with an attached script) to promote the use of Bextra to reduce the risk of DVTs to surgeons, even though the Regional Manager knew that Bextra had not been approved by the FDA to reduce the risk of DVTs.

54. In at least one region, **PHARMACIA** sales representatives and managers implemented this instruction and promoted Bextra to physicians to reduce the risk of DVTs during and after surgery, without disclosing to these physicians the safety concern that the FDA has raised concerning the use of Bextra in surgery, or the fact that the FDA had concluded that no decrease in the side effects of surgery such as DVTs had been shown from the use of Bextra.

E. PHARMACIA's Promotion of Bextra with False and Misleading Safety and Comparative Claims

55. **PHARMACIA** sales representatives promoted Bextra by telling physicians to replace Vioxx with Bextra even though Vioxx had an FDA-approved acute pain indication and Bextra did not; and by telling physicians that Bextra was safer and more effective than Vioxx, despite the fact that **PHARMACIA** knew there were no head-to-head studies of Bextra and Vioxx for the approved uses of Bextra that showed that Bextra was safer or more effective.

56. **PHARMACIA** sales representatives promoted Bextra with false and misleading claims of safety, including that Bextra had no dose proportional increase in hypertension and edema, that “there is not one shred of evidence showing a CV concern with Bextra,” that Bextra had no cardiovascular risks unlike Vioxx, and that Bextra had placebo-like side effects.

57. For example, on or about January 16, 2004, a **PHARMACIA** Regional Manager circulated to other **PHARMACIA** managers in the Northeast a Product Action Guide that listed as core messages for the promotion of Bextra that “Vioxx’s problems are not a class effect. [. . . With] Bextra there is no dose proportional response with hypertension and edema.”

58. **PHARMACIA** sales representatives implemented this instruction and promoted Bextra to physicians with the claims that “Vioxx’ problems are not a class effect” and “there is no dose proportional response with hypertension and edema” with Bextra, even though these claims were not proven nor supported by Bextra’s label. In fact, the evidence in Bextra’s label demonstrates that it does cause a dose proportional increase of hypertension and edema.

F. PHARMACIA's Promotion of Bextra Through Falsely Claiming that Physicians Had Asked for Information About Unapproved Uses

59. PHARMACIA's sales representatives also created sham physician requests for medical information about unapproved uses in order to send unsolicited information to physicians about unapproved uses and dosages of Bextra.

60. In or about June 2002, in or about November 2003, and at other times, PHARMACIA managers instructed members of the sales force to send out unsolicited letters known as Medical Inquiry Letters (also known as the "Medical Letter" or "Medical Inquiry Response") to, among others, groups of physicians who prescribed a lot of Vioxx. These letters were issued by PHARMACIA as if they were responses to physicians' unsolicited inquiries and contained medical information relating to unapproved uses and dosages of Bextra.

61. PHARMACIA managers instructed their sales teams to send the Medical Inquiry Letters to top Vioxx prescription writers who had not made requests for the letters, including by instructing their teams to send them to "Every Vioxx Loyalist," even though they knew it was improper to send these letters unsolicited and knew that the letters, which appeared to be a response to an unsolicited inquiry, were a disguise for improper promotion.

62. At the direction of their managers, PHARMACIA sales representatives sent unsolicited Medical Letters with information to support the use of Bextra for unapproved uses and dosages to physicians.

63. In the Medical Letters, PHARMACIA did not disclose the FDA's safety concern with the use of Bextra for unapproved uses, such as acute pain, and unapproved dosages. Nor did PHARMACIA disclose that the FDA raised a concern about the use of Bextra in surgery

based upon the CABG I study and the excess of serious cardiovascular thromboembolic events in the Bextra (after parecoxib) arm of the study.

G. PHARMACIA's Off-Label Promotion of Bextra By Distribution of Samples for Unapproved Uses/Doses

64. PHARMACIA's sales force provided promotional samples of Bextra to surgeons and other medical prescribers who had no FDA-approved use for the Bextra samples, including by providing dosages that were unapproved for the uses for which the physicians were expected to use the samples.

65. PHARMACIA distributed samples of Bextra, including 20 mg samples, to physicians whom PHARMACIA knew would not prescribe it for approved uses or dosages, such as oral surgeons, dentists and other surgeons.

66. PHARMACIA allocated approximately 25% of all Bextra samples to 20 mg samples, even though PHARMACIA knew that the primary dysmenorrhea market (the only market for which Bextra at 20 mg was FDA-approved) was only a tiny percentage of the total potential sales (approximately 1-3%).

67. PHARMACIA allocated 20 mg samples to sales representatives who did not call on any type of doctor who treated primary dysmenorrhea and thus who had no FDA-approved use for 20 mg doses of Bextra.

68. PHARMACIA used a national computer program to direct the sales force on how to utilize these free samples, which instructed sales representatives to increase use of 20 mg samples for certain physicians, such as rheumatologists and orthopaedic surgeons, even though these physicians had no approved use for such samples.

H. Use of Purportedly Independent Continuing Medical Education to Promote Bextra for Unapproved Uses and Dosages

69. PHARMACIA also funded purportedly independent continuing medical education programs (“CME”) with the stated purpose of disseminating messages promoting Bextra for unapproved uses, including specifically for acute pain and surgical pain.

70. PHARMACIA accomplished this by incorporating CME planning into its marketing messaging strategy for Bextra. Among the practices PHARMACIA employed was to hire advertising agencies to prepare standard promotional slides for Bextra, and then had these slides certified by other vendors as “CME.” It then caused these Bextra slide sets to be distributed to the “advocates” it had trained so that they could use the slides for CME events as well.

71. PHARMACIA’s headquarters-based marketing teams also created annual medical education plans in which they reflected the intention to “leverage CME” to provide data beyond the approved label. The plans listed the specific messages for Bextra to be relayed, including messages such as Bextra power for “Acute pain, Opioid-sparing.”

72. In 2002 alone, PHARMACIA funded CME programs for Bextra designed to reach 30,000 physicians, including in many instances with the unapproved messages.

I. Promotion of Bextra for Unapproved Uses and Dosages by Supporting and Drafting Publications

73. PHARMACIA also promoted Bextra for unapproved uses and dosages through a “publication strategy” whereby PHARMACIA initiated, funded, sponsored and sometimes drafted or hired medical writer vendors to draft articles about Bextra for unapproved uses and dosages in order to promote these uses and dosages, without always appropriately disclosing

PHARMACIA's role in the process.

74. **PHARMACIA** implemented a “manuscript development” process whereby a core team at **PHARMACIA** would plan potential publications and recruit authors for them. Some of those listed in the publication plans were listed with authors as “TBD” (to be determined) or “TBC” (to be chosen).

75. **PHARMACIA** also created an overall list of its goals for this process, which included relaying unapproved messages for Bextra such as “Acute Pain: BEXTRA Provides Rapid, Powerful Pain Relief in surgical pain.”

COUNT ONE

**(Introduction into Interstate Commerce of a Misbranded Drug:
21 U.S.C. §§ 331(a), 333(a)(2) & 352(f))**

76. The allegations contained in paragraphs 1 through 75 are realleged and incorporated herein as if set forth in full.

77. Between February 2002 and April 2005, in the District of Massachusetts and elsewhere, the defendant,

PHARMACIA & UPJOHN COMPANY, INC.

with intent to defraud and mislead, did introduce, deliver for introduction, and cause the introduction into interstate commerce, into Massachusetts and elsewhere, quantities of Bextra, a drug within the meaning of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 321(g), which was intended for use for the treatment of acute pain, surgical pain, other unapproved uses, and at unapproved dosages, which was misbranded within the meaning of 21 U.S.C. § 352(f)(1), in that it lacked adequate directions for such uses.

All in violation of 21 U.S.C. §§ 331(a), 333(a)(2), and 352(f)(1).

FORFEITURE ALLEGATIONS

1. As a result of the violation of Title 21, United States Code, Sections 331(a), 333(a)(2), and 352(f)(1) set forth in this information, defendant,

PHARMACIA & UPJOHN COMPANY, INC.

shall forfeit to the United States of America any quantities of Bextra, which between February, 2002, and April 5, 2005, were misbranded when introduced into or while in interstate commerce, or while held for sale (whether or not the first sale) after shipment in interstate commerce, or which may not, under the provisions of Title 21, United States Code, Section 331, be introduced into interstate commerce.

2. If any of the property subject to forfeiture, as a result of any act or omission of the defendant:

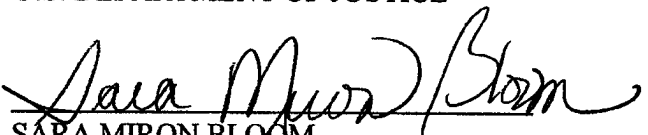
- (a) cannot be located upon the exercise of due diligence;
- (b) has been transferred or sold to, or deposited with, a third party;
- (c) has been placed beyond the jurisdiction of the Court;
- (d) has been substantially diminished in value; or
- (e) has been commingled with other property which cannot be divided without difficulty;

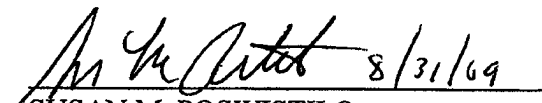
it is the intent of the United States, pursuant to Title 21, United States Code, Section 853(p), to seek forfeiture of any other property of the defendant up to the value of the property subject to forfeiture, that is \$105,000,000.

All pursuant to Title 21, United States Code, Sections 334 and 853 and Title 28, United States Code, Section 2461(c).

MICHAEL K. LOUCKS
ACTING UNITED STATES ATTORNEY
DISTRICT OF MASSACHUSETTS

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